REMARKS

Claims 65-71 were pending in the subject application. In this amendment, Applicants have amended claim 65. Claims 65-71 are now pending in the subject application.

Claim 65 has been amended to specify clarify that "the lyophilized pharmaceutical composition has a pH from about 3 to about 5 when reconstituted with water."

Support for the amendment to claim 65 can be found in the original specification at, for example, page 24, ¶ [0087] and page 26, ¶ [0093].

No new matter is added by these amendments, and Applicants respectfully request their entry.

Applicants wish to thank Examiner Peselev and her colleague, Examiner Roy P. Isaac, for the courtesy of a personal interview held at the United States Patent and Trademark Office on December 11, 2007 ("the Interview") with Applicants' Attorneys David L. Kershner (Reg. No. 53,112) and Adrian G. Looney (Reg. No. 41,406). Also present at the Interview were two Pfizer Inc. scientists, Peter Rose and Paul Luner, Ph.D.

Independent claim 65 of Applicants' invention is directed to a pharmaceutical composition comprising: dalbavancin containing MAG in an amount of less than about 3 mole percent; and at least one effective stabilizer; wherein the composition is lyophilized; and wherein the lyophilized pharmaceutical composition forms an aqueous solution having a pH from about 3 to about 5.

At the Interview Applicants discussed the differences between U.S. Patent No. 5,750,509 to Malabarba et al. ("the '509 Malabarba Patent") and the pharmaceutical formulation claimed in the subject application. Applicants also discussed how the pH of dalbavancin is influenced by its method of isolation, i.e., in order to prepare dalbavancin having an acidic pH, it must be isolated under acidic conditions. Applicants noted that the '509 Malabarba Patent is concerned with the preparation of compounds not with formulating the disclosed compounds. In contrast Applicants' claimed invention is directed to a pharmaceutical formulation which is a separate endeavor from that of making individual compounds. Although, Malabarba refers to compositions, it is only in a very general manner and is indicative of the fact that the '509 Malabarba patent is concerned with compound preparation and not formulation preparation as is the case in the instant application.

The Examiner rejected the instant application in part based upon the disclosure of a process to make dalbavancin in Example 10 of the '509 Malabarba Patent. At the Interview Applicants discussed the process to make a dalbavancin according to Example 10 of the '509 Malabarba Patent using a process flow diagram. A copy of the process flow diagram for Example 10 in the '509 Malabarba Patent is attached hereto as Exhibit 1. As discussed with Examiners Peselev and Isaac (and shown in Exhibit 1), all of the process steps of Example 10 of Malabarba are carried out at a pH of about 7 or higher, and the last process step (isolation step) of Example 10 is carried out at a pH of about 7. Applicants noted that this form of dalbavancin would have a pH of about 7, because it was isolated at pH 7. In other words, dissolving dalbavancin isolated at pH 7 in deionized water, without any additional components or pH adjustment, would provide an aqueous solution having a pH of about 7. The '509 Malabarba Patent does not provide any further teaching concerning pH or adjustment of the pH of 7 used to prepare Example 10.

Applicants also discussed at the Interview a process flow diagram of Example 9 of the subject application used to prepare dalbavancin used in the claimed pharmaceutical formulations. A copy of the process flow diagram is attached hereto as Exhibit 2. As discussed with Examiners Peselev and Isaac (and shown in Exhibit 2), dalbavancin made according to Example 9 of the subject application involves a multi-step process and includes four separate pH adjustments throughout the process to maintain the dalbavancin at a low pH. The first step is the saponification of the dalbavancin at a pH of about 12 followed by a pH adjustment by the addition of HCl to provide a mixture having a pH of 3. Subsequent steps are carried out at a pH from 2.8 to 4.1. The last process step in Example 9 of the subject application includes the pH adjustment to 2.63 followed by the isolation of the dalbavancin with a pH of 3. The final dalbavancin isolated is a dry powder and Applicants noted that this form of dalbavancin if reconstituted in water would have a pH of about 3 since it was isolated at pH 3. In other words, dissolving dalbavancin isolated at pH 3 in deionized water would provide an aqueous solution having a pH of about 3 and not an aqueous solution having a pH of about 7 if the dalbavancin from Example 10 of the'509 Malabarba Patent is utilized.

At the Interview Examiner Peselev said it was not clear if the dalbavancin used to prepare composition D in Table 4 in U.S. Patent No. 7,119,061 to Stogniew et al. ("the '061 Stogniew Patent) was the same form disclosed in Example 10 of the '509 Malabarba Patent or some other form. Applicants discussed at the Interview the differences between the dalbavancin used to prepare composition D in the '061 Stogniew Patent and dalbavancin compound (not composition) prepared in Example 10 of the '509 Malabarba Patent.

Applicants would like to clarify for the record that the form of dalbavancin used in making Composition D in Table 4 (column 23, lines 10 to 27) of the '061 Stogniew Patent is not the same form of dalbavancin as disclosed in Example 10 (column 32, lines 20 to 38) of the '509 Malabarba Patent, because Malabarba's form of dalbavancin is isolated at a pH of 7. Therefore a solution prepared using dalbavancin isolated at pH 7 (e.g., the form of dalbavancin prepared in the '509 Malabarba Patent's Example 10) and deionized water would have a pH of about 7. Accordingly, the dalbavancin disclosed in the Example 10 of the '509 Malabarba Patent is different from that described in the subject application and in the '061 Stogniew Patent because it was isolated at a higher pH from that of the dalbavancin prepared in the subject application and the '061 Stogniew Patent. (See Exhibit 1 for the dalbavancin process employed in Example 10 of the Malabarba Patent; and Exhibit 2 for the dalbavancin process employed in '061 Stogniew Patent and in the instant application.)

At the Interview Examiner Peselev also stated that it was not clear if the pH range recited in the claims of the subject application referred to the pH of the solid form of the pharmaceutical composition or a solution form. Applicants noted that independent claim 65 of the subject application already recites that "the composition is lyophilized" which specifies that the claimed composition is in a solid form. Applicants also noted that the recitation of a pH range of "from about 3 to about 5" refers to the pH of an aqueous composition when the lyophilized pharmaceutical composition of the invention is dissolved in aqueous media. Nevertheless, Applicants agreed to clarify the claimed subject matter, and independent claim 65 the subject application has been amended to specify that

"the lyophilized pharmaceutical composition forms an aqueous solution having a pH from about 3 to about 5."

Applicants will now provide additional remarks for the rejections from the September 10, 2007 final Office Action ("the final Office Action").

I. Rejection of Claims 65-71 under 35 U.S.C. § 102(b)

In the final office action the Examiner rejected claims 65-71 under 35 U.S.C. § 102(b) as allegedly being anticipated by the '509 Malabarba Patent. The Examiner stated that "Malabarba et al disclose composition comprising dalbavancin and a stabilizer (column 28, lines 9-12) and also disclose said composition in the form of a powder (column 28, line 13). Malabarba et al further disclose the combination of dalbavancin in combination with sugar, such as lactose (column 27, line 54-56)." The Examiner asserted that "[t]he claimed compositions are anticipated by Malabarba et al since the composition disclosed by Malabarba et al would be expected to have inherently pH of about 3." Applicants respectfully traverse.

Applicants submit that the '509 Malabarba Patent does not disclose, either expressly or inherently, a pharmaceutical composition comprising dalbavancin and at least one effective stabilizer, wherein the composition pH is about 3 to about 5 as recited in the claims of the subject application. Rather, the '509 Malabarba Patent relates to amide derivatives of antibiotic A 40926. The Examiner cited Example 10 in the '509 Malabarba Patent for a process of making dalbavancin having a pH of 3. Applicants discussed in the Interview (see above) and shown in Exhibit 1 that the process steps of Example 10 of the '509 Malabarba Patent are carried out at a pH of about 7 or higher and the last step (isolation step) is carried out at pH of about 7. Therefore a composition containing the form of dalbavancin disclosed in Example 10 of the '509 Malabarba Patent (i.e., isolated at pH 7) will have a pH of about 7 when said composition is dissolved in deionized water. The '509 Malabarba Patent does not disclose any other form of dalbavancin which has been isolated at a pH of less than 7.

During the Interview, Examiner Peselev indicated that Composition D in Table 4 (column 23, lines 10 to 27) of the '061 Stogniew Patent has a pH of 3.01. Examiner Peselev indicated that this form of dalbavancin appeared to be the same form as disclosed in Malabarba. As discussed at the Interview and above, dalbavancin used in making Composition D in the '061 Stogniew Patent is prepared at a different pH from the dalbavancin disclosed in Example 10 (column 32, lines 20 to 38) of the '509 Malabarba Patent, because Malabarba's form of dalbavancin is isolated at a pH of 7. Therefore a solution prepared using dalbavancin isolated at pH 7 (e.g., the form of dalbavancin prepared in the '509 Malabarba Patent's Example 10) and deionized water would have a pH of about 7. In contrast, Composition D in the '061 Stogniew Patent has a pH of 3.01

"[R]ejections under 35 U.S.C. 102 are proper only when the claimed subject matter is identically disclosed or described in 'the prior art'." *In re Arkley, Eardley, and Long*, 455 F.2d 586 (C.C.P.A. 1972. A prior art reference anticipates a claim if the reference discloses, either expressly or inherently, all the limitations of the claim. *EMI Group N. Am. v. Cypress Semiconductor*, 268 F.3d. 1342, 1350 (Fed. Cir. 2001).

The '509 Malabarba Patent does not disclose either expressly or inherently any composition containing dalbavancin wherein the composition pH is from about 3 to about 5 as recited in independent claim 65 of the subject application. Therefore, claim 65 and claims 66-71 which depend directly or indirectly upon claim 65 of the subject application are not anticipated by the '509 Malabarba Patent.

In view of the above, Applicants submit that claims 65-71 of the subject application are not anticipated by the '509 Malabarba Patent, and request that the rejection of claims 65-71 under 35 U.S.C. § 102(b) be withdrawn in view of Applicants' remarks.

II. Rejection of Claims 65-71 under 35 U.S.C. § 103(a)

In the final office action the Examiner rejected claims 65-71 under 35 U.S.C. § 103(a) as allegedly being obvious over the '509 Malabarba Patent for the reasons set forth in the office action. In particular, the Examiner stated that "if there are any differences between the claimed composition and the prior art composition [of Malabarba], the differences would appear to be minor in nature and the claimed composition, which falls within the scope of the prior art's disclosure, would have been prima facia obvious from the said prior art's disclosure to a person having ordinary skill in the art at the time the claimed invention was made." Applicants respectfully traverse.

As discussed at the Interview, the stability of dalbavancin is affected by pH. That is, dalbavancin is less stable at lower pH and more stable at higher pH. In view of the decreasing stability at lower (acidic) pH, a pharmaceutical formulator seeking to make a stable dalbavancin-containing pharmaceutical composition of the present invention based upon the teaching of the '509 Malabarba Patent would need some reason to make a dalbavancin composition acidic, i.e., having a pH of less than 7. However, the skilled formulator would not find any reason in the '509 Malabarba Patent to make an acidic form of a dalbavancin composition. The '509 Malabarba Patent does not disclose any form of dalbavancin isolated at a pH of less than about 7; moreover, the '509 Malabarba Patent does not teach or even suggest any dalbavancin composition having a pH of less than 7.

Therefore, in view of the instability of dalbavancin at low pH and further view of the lack of teaching or suggestion in the '509 Malabarba Patent to make or use a dalbavancin composition at pH of less than 7, one of skill in the art would find no teaching, suggestion or motivation to make any dalbavancin-containing composition having a pH of less than 7. Furthermore, there is no teaching or suggestion in the '509 Malabarba Patent to maintain a low pH as the dalbavancin is isolated. This teaching is found in Applicants claimed invention not the '509 Malabarba Patent.

"Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so." MPEP § 2143.01.I (citing *In re Kahn*, 441 F.3d 977, 986 (Fed. Cir. 2006)).

As explained above, the '509 Malabarba Patent does not teach or suggest a dalbavancin composition having a pH less than about 7. Moreover, the '509 Malabarba Patent provides no reason to modify any dalbavancin composition in order to achieve a dalbavancin composition having a pH of less than 7, especially in view of the decreased stability of dalbavancin at low pH as discussed in the Interview and noted above.

Applicants respectfully submit that one of skill in the art would find no suggestion or motivation in the '509 Malabarba Patent to make or use a dalbavancin-containing composition where the pH of the composition is less than 7, let alone where the pH of the composition is from about 3 to about 5 as recited in independent claim 65 of the subject application. Accordingly, claims 65 and claims 66-71 which depend directly or indirectly upon claim 65 are not obvious over the '509 Malabarba Patent.

In view of the above, Applicants submit that claims 65-71 are not obvious over the '509 Malabarba Patent, and request that the rejection of claims 65-71 under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

Applicants respectfully request prompt consideration of the pending claims and early allowance of the application. No additional fee is believed due. However, if any fee is due, the Examiner is authorized to charge the fee to Applicants' Deposit Account No. 16-1445.

If the Examiner wishes to comment or discuss any aspect of this application or response, Applicants' undersigned attorney invites the Examiner to call him at the telephone number provided below.

Respectfully submitted,

Date: January 3, 2008

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Exhibits

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Exhibit 1

U.S. Patent No. 5,750,509 to Malabarba et al.

Dalbavancin work-up described in Example 10 of Malabarba et al.

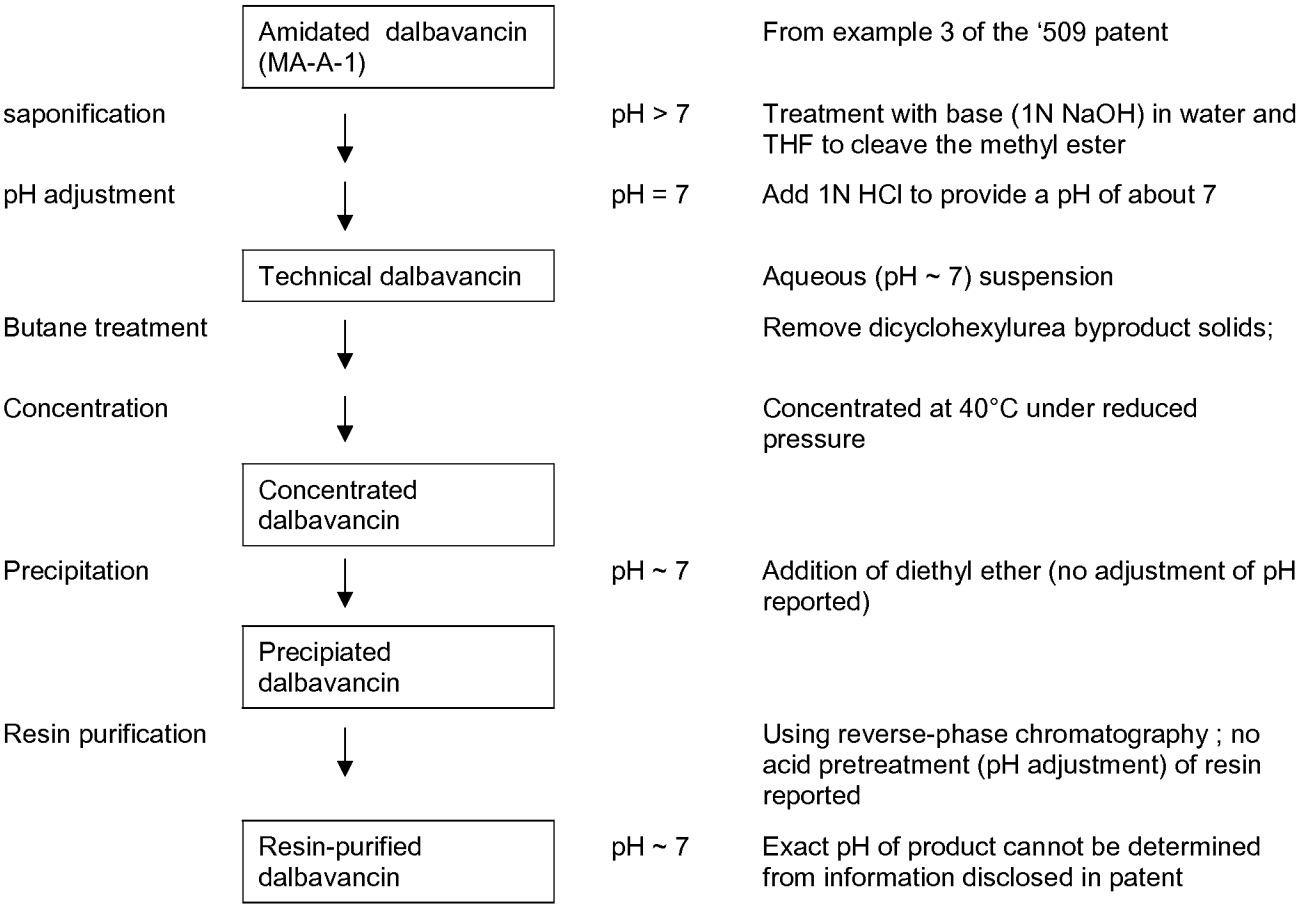

Exhibit 2

U.S. Patent Application No. 10/829,068

Dalbavancin work-up described in Example 9 of the'068 application and Example 11 of U.S. Patent No. 7,119,061 to Stogniew et al.